



I am Mike Dubinsky, Director, Regulatory Compliance, Alpha Therapeutic Corporation. On behalf of Alpha I wish to thank the Food and Drug Administration for the opportunity and the forum to offer some views from the standpoint of a member of regulated industry about how FDA might improve its regulatory effectiveness. Alpha Therapeutic Corporation is located at 5555 Valley Boulevard in Los Angeles California. Alpha holds a license for several therapeutic biologic products derived from human plasma, has a number of licensed plasma donor centers in the United States and also manufactures several medical device products subject to FDA regulation. In addition Alpha is involved as the holder of an approved NDA. Alpha therefore sees itself as a full stakeholder in the matter of interacting with the FDA. We do so daily and across a wide range of product. FDA offered seven questions related to each of the objectives and Alpha wishes to offer comment on four of the areas.

1. Submission Review Process - The FDA's available guidance and materials on what to submit is not ostensibly lacking, but the opportunity to interact with staff to discuss the day to day application of the principles described in the submission process is where the needs seem to arise. The application of the submission guidance differs across product line areas and therefore the opportunity to speak with FDA staff relative to preparing the submission becomes important. Sometimes the opportunity to speak to an advisor who knows the system but is not directly related to the day to day review process allows for an exchange of information which is complete but does not disturb the review process. The Center For Devices and Radiological Health manufacturers assistance group is an example. CBER also has a manufacturers assistance group and they too are most helpful. The expansion and enhancement of such support units allows for better communication and understanding. For the actual submission review process the policy of integrating consumer safety officers into the review divisions of FDA represents a sound approach. For Alpha having a point of contact person who is responsive, and able to respond, has proven to be one of the most effective tools that FDA can bring to bear to enhance the submission and application review process.

2. Work to ensure that Products, both domestic and foreign are of high quality. Pursuing initiatives which have as their end result, criteria accepted internationally is a goal which would well serve the biological product industry and the FDA goals. The FDA has established a sound track record for participation in the ICH projects. Those experiences have set down understood and accepted pathways to follow as product development and application submission are approached. Applying a similar mindset to dealing with other aspects of product regulation also represents an opportunity to ensure consumer protection yet add efficiency to the regulatory process. We see initiatives in this area, especially in dealing with devices but ~~we~~ there appears to be a reluctance to adopt different approaches. Having recently worked through the experience of pursuing a device authorization using the EEC approach we can say that while different it works and offers the consumer protection elements that are necessary. That approach involves the Notified Body assessment of a product and the

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manufacturers quality system approach to manufacture. FDA has described both third party and first party approaches to the area of inspections. Both of these concepts have merit but there must be an incentive to participate. That aspect has been elusive as we understand it. Alpha would offer the thought that if the FDA wishes to successfully pursue such initiatives it must be prepared to take a risk in terms of trust and respect for the industries it regulates. Industry must be prepared to take risks as it pursues new products and innovative approaches to delivering those products. While we recognize that the public health mission of FDA must be first, there is what could be termed a balance point, where CBER and its colleagues in the FDA can find common points of agreement in terms of our business interactions. For example if one Center in the FDA can undertake a program of announced inspections, where investigators communicate fully during an inspection and even note that immediate corrective actions have occurred, why can't other FDA units take the same risk?

3. Scientific and Technical Expertise - Partnerships with academia and technical institutions is a mechanism that FDA has used and could use more effectively to cultivate and maintain scientific and technical expertise. Perhaps FDA could establish "Chairs" at academic institutions with the institutions then providing laboratory facilities and opportunities in enhancing the regulatory sciences. The FDA has undertaken such an effort in the food program area. Could it work in other?

4. Burdens on the Application Review Process - Effectiveness in the review process can be a function of an effective systems approach. Industry is expected to have one in place. FDA can benefit from employing the same approaches that are expected of industry. Having procedures in place which are understood, followed and which staff are trained against can go a long way to making any process less burdensome. We recognize that CBER has procedures in place and is working on a fuller expression of the Managed Review Process. As with industry validating the system to show that it can reproducibly result in a quality product, meeting customer expectations and delivered on time would seem important. In theory the FDA system does have such approaches built in but the application and management of those activities is the key to success. Alpha would encourage adopting a policy of measuring effectiveness in ways that can be communicated to the constituencies with which FDA interacts.

Alpha recognizes that concepts such as the ones we reflect on today are just that, concepts. The theme of working together in a manner whereby the regulator and regulated industry better communicate and are better understood is a complex undertaking. Having said that Alpha would offer individually or through the appropriate channels to be a participant in a CBER managed review training seminar. Specifically to bring to the training table the experiences and concerns, and factors which accompany the application review process, from another vantage point.

Thank you for the opportunity to comment.